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Projected Reduction in Healthcare Costs in Belgium After Optimization of Iodine Intake: Impact on Costs Related to Thyroid Nodular Disease

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Background: Several surveys in the last 50 years have repeatedly indicated that Belgium is affected by mild iodine deficiency. Within the framework of the national food and health plan in Belgium, a selective, progressive, and monitored strategy was proposed in 2009 to optimize iodine intake. The objective of the present study was to perform a health economic evaluation of the consequences of inadequate iodine intake in Belgium, focusing on undisputed and measurable health outcomes such as thyroid nodular disease and its associated morbidity (hyperthyroidism).
Methods: For the estimation of direct, indirect, medical, and nonmedical costs related to thyroid nodular diseases in Belgium, data from the Federal Public Service of Public Health, Food Chain Safety and Environment, the National Institute for Disease and Disability Insurance (RIZIV/INAMI), the Information Network about the prescription of reimbursable medicines (FARMANET), Intercontinental Marketing Services, and expert opinions were used. These costs translate into savings after implementation of the iodization program and are defined as costs due to thyroid nodular disease throughout the article. Costs related to the iodization program are referred to as program costs. Only figures dating from before the start of the intervention were exploited. Only adult and elderly people ($\geq$18 years) were taken into account in this study because thyroid nodular diseases predominantly affect this age group.
Results: The yearly costs due to thyroid nodular diseases caused by mild iodine deficiency in the Belgian adult population are ~€38 million. It is expected that the iodization program will result in additional costs of ~€54,000 per year and decrease the prevalence of thyroid nodular diseases by 38% after a 4–5-year period. The net savings after establishment of the program are therefore estimated to be at least €14 million a year.
Conclusions: Optimization of iodine intake in Belgium should be quite cost effective, if only considering its impact on nodular thyroid disease. There are likely added benefits relating to more optimal thyroid hormone influenced brain development that are more difficult to estimate but may be even more important.

Introduction

Despite a worldwide successful implementation of iodine fortification and supplementation programs over the last 4 decades, iodine deficiency remains a public heath problem in Europe. In 2004, it was estimated that of the 2 billion people around the world at risk of iodine deficiency, 20% live in Europe (1). Over the last 2 decades, extraordinary progress has been achieved in decreasing the prevalence of iodine deficiency disorders by increasing the number of people with access to iodized salt (2). However, this has not been the case in Europe, where, compared to other regions in the world, iodized salt coverage is low, reaching only 27% of households (3).

Several surveys in the last 50 years have repeatedly indicated that Belgium is affected by mild iodine deficiency (MID) (4–6). In 1998, a representative survey in Belgian school children showed a median urinary iodine concentration of 80 μg/L (4), lower than the optimal urinary median values of 100–199 μg/L in the population (7). Consequently, optimizing iodine intake was chosen among several other nutritional issues as a priority by the Ministry of Health in its "National

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Nutrition and Health Plan for Belgium" for the period 2005–2010. Within the framework of this plan, a selective, progressive, and monitored strategy was proposed to optimize iodine intake in Belgium.

In an agreement between the bread sector and the Ministry of Health, Food Chain Safety and Environment, signed in April 2009, it was established that from then onward, all breads produced would be fortified with iodized salt (10–15 ppm). This choice stems from the fact that it is easier to control and regulate the iodine content in one food item rather than in several items. Also the implementation is easier as bread is mainly made for local consumption. A selective approach is particularly relevant in countries affected by MID like Belgium to avoid an increase of iodine beyond the optimal intake.

The fortification of bread with iodine has already been implemented with success in other countries like The Netherlands (8) and Denmark (9,10). To be truly selective this strategy implies that other potential sources of iodine should be avoided or at least maintained constant to avoid uncontrolled variation of iodine intake in the population.

Because a transitory increase of hyperthyroidism may occur in case of rapid increase of iodine intake, in particular in the elderly population with multinodular goiter, a progressive, step-by-step increase of iodine intake is preferred (11). This notion is particularly important because small variations in daily iodine intake are sufficient to affect thyroid function (12–14).

The results of the national food consumption survey in adults (2004) showed that the bread consumption amounts to 120 g/day (P25: 82 g/day; P75: 150 g/day) and is the most important source of salt intake in Belgium (15).

Considering an estimated daily iodine intake of 80 μg of iodine in Belgium (4), the strategy is aiming at an initial increase in daily iodine intake of 30 μg during the first 5 years. In a second phase, taking into account the results of the monitoring program, a further increase of 40 μg of daily iodine intake is aimed at to attain an average intake of 150 μg of iodine over a period of 10 years (16).

The drawback of a selective and progressive strategy is that some people, who only eat very little bread, don't benefit from the intervention such as weaning infants, ethnic groups, people on a weight-loss or low-carbohydrate diet, and persons with celiac disease.

Monitoring will be based on the determination of urinary iodine concentrations in a representative sample of school-aged children and pregnant women every 4–5 years, as well as on the evaluation of thyroid function in pregnant women and thyroid-stimulating hormone (TSH) concentrations in newborns. Data on neonatal TSH will be collected from the six reference centers performing the screening of congenital hypothyroidism in Belgium.

Further, the possible increase of any adverse effects (iodine-induced hyperthyroidism), due to the implementation of the program, will be monitored via follow-up of the use of anti-thyroid drugs and radio-iodine (I-131) therapy in Belgium.

Previous studies have shown that iodine fortification is both cost effective and has a high benefit/cost ratio, particularly if iodine deficiency is severe or moderate (17).

It is believed that a program for the control of MID in Belgium is worthwhile only, in health economic terms, if the societal costs of the program are lower than the saved costs that result from the correction of the deficiency.

The health economic advantages of avoiding endemic goiter and mental retardation in case of severe iodine deficiency are quite obvious. On the contrary, the benefit of correcting MID is less obvious. The main consequences of MID in the adult population are a high prevalence of multinodular goiter and thyroid nodules, which may be responsible of hyperthyroidism (18–23). In addition, it has been suggested that iodine supplementation improves cognition in mildly iodine-deficient children (24).

The objective of the present study was to perform, from the perspective of the healthcare sector (combining patient and insurer cost), a health economic evaluation of the consequences of inadequate iodine intake in Belgium, focusing on undisputed and measurable health outcomes such as nodular disease and its associated morbidity (hyperthyroidism) in the adult population. Such a health economic estimation is useful for policy makers to appraise whether the allocated resources for optimizing iodine intake in Belgium are well spent.

Material and Methods

Costs due to the iodization program

Total iodization program costs (PC) include costs of social marketing to attain public acceptance of (or preference for) the fortified food, costs of quality control and quality assurance of salt iodization in bread by producers and of governmental monitoring and evaluation activities, costs of any campaign or publication stimulating iodine supplementation, and costs of the monitoring program for a period of 4–5 years. Monitoring of TSH in newborns is free as the data are available already. The implementation of the program does not include costs of supplying iodized salt as this is already on the market, technology cost, and costs for equipment, land, labor, maintenance, and electricity. The small difference of price between iodized salt and noniodized will not affect the cost of bread production and will not increase the price of the product.

In Belgium the salt content of bread is regulated by law and monitored on regularly by the Federal Agency for Safety of the Food Chain (FASFC). From April 2009 onward, FASFC simultaneously verifies the concentration of iodine in salt used by the bakers for the manufacture of bread, by checking the label and/or product information of the iodized salt used. These concentrations as such are not analyzed.

Therefore these costs are negligible.

Costs related to thyroid nodular disease in Belgium

Costs related to thyroid nodular disease translate into savings after implementation of the iodization program and are defined as costs due to thyroid nodular disease (TC) throughout the article.

Only adult and elderly people ($\geq$18 years) were taken into account in this study because thyroid nodular disease predominantly affects this age group. Further, only prevention of nodular disease (multinodular goiter and thyroid nodules) and its associated morbidity (hyperthyroidism) was included in this study. Some other saved costs (due to better cognition, higher productivity, etc.) (24–28) are important too but very difficult to assess and therefore excluded, which makes the results more conservative. Hypothyroidism is excluded in this study because this pathology is mainly due to autoimmune diseases, which are not related to iodine deficiency. Epidemiological studies have shown that hypothyroidism is more prevalent in populations with a high iodine intake (20,29–32) or in severe iodine deficiency (2). Mild-to-moderate iodine deficiency is not associated with hypothyroidism (20), although the exact association between the level of iodine intake in a population and the occurrence of hypothyroidism is not clear. Finally, costs related to work disability, including days of absence from employment, were not included in this study.

No data are available in Belgium about the true prevalence of thyroid nodular diseases (including multinodular goiter and thyroid nodules) in the adult population, as no studies were performed in the past.

Therefore, prevalence data from a country with as much as possible the same demographic characteristics, the same salt iodization history, same intervention program, and same iodine status, food consumption pattern, and hospitalization rate for iodine deficiency disorders were used.

In Denmark, iodization of salt was prohibited from 1982 until 1998, when an optional iodization of salt was initialized. This led to only a limited use of iodized salt, so from the year 2000 iodization of all household salt and salt used in the bread industry was made mandatory to a level of 13 ppm iodine (33). Denmark prospectively evaluated the effect of 4 years of mandatory iodization of salt (13 ppm iodine) on thyroid volume in two regional areas with, respectively, mild (the northern part of Copenhagen, eastern Denmark; median urinary iodine concentration of 61 μg/L before mandatory fortification) and moderate (Aalborg, western Denmark; median urinary iodine concentration of 45 μg/L before mandatory fortification) iodine deficiency.

Two separate cross-sectional studies were performed before ($n = 4649$) and after ($n = 3570$) the iodization. Women aged 18–22, 25–30, 40–45, and 60–65 years and men aged 60–65 years were examined. Before the iodization, 17.6% of the participants had thyroid enlargement, whereas, after the iodization, this percentage decreased to 10.9% (33). This is a relative decrease of 38%.

Denmark seems to be the country where salt iodization history is best comparable with the situation in Belgium. A comparison of demographic information, hospitalization rate for thyroid disorders, and food consumption of some key products between Belgium and Denmark can be found in Table 1.

As a starting point for this study the prevalence of thyroid enlargement in Denmark in the adult population (17.6%) before mandatory iodization was used to estimate the prevalence of thyroid disorders (multinodular goiter and thyroid nodules) in the Belgian population. Thyroid enlargement in the Danish studies was defined as a thyroid volume greater than 18 mL for women and 25 mL for men. These values correspond to the mean + 3 standard deviation values in iodine-sufficient populations (33).

It could be derived that before the introduction of the salt iodization intervention in 2009, about 1,490,892 adult persons were suffering from multinodular goiter and thyroid nodules

Table 1. Demographic Data, Hospitalization Rate for Thyroid Disorders, and Food Consumption of Some Key Products in Denmark and Belgium

Demographic indicators	*Belgium*	*Denmark*
Total population		
Males	5,224,309	2,712,666
Females	5,442,557	2,763,125
Total adult population		
Males	4,102,708	2,089,836
Females	4,368,270	2,170,471
Women per 100 men	104.2	101.9
Life expectancy at birth		
Males	77.46	76.26
Females	83.51	80.70
Proportion of the population		
Aged 20–39 years	26.0	25.2
Aged 40–59 years	28.4	27.9
Aged 60–79 years	17.9	18.3
Aged 80 years and more	4.7	4.1
Crude rate of net migration	4.86	5.32
Crude birth rate	11.67	11.84
Crude death rate	9.49	9.94
Food consumption		
Consumption of fish and seafood	24 ± 25 g/day	18 ± 19 g/day
Consumption of dairy (products)	203 ± 188 g/day	386 ± 283 g/day
Used dietary assessment method	2×24-hour recall	7-day record
Hospitalization rate		
Number of hospitalizations per 100,000 (whole population 2006)	17,770	21,666
Number of hospitalizations for thyroid disorders per 100,000 (adult population 2006)	70.5	58.7

Sources: EUROSTAT 2008, Federal Public Service of Health in Belgium, Stat Bank in Denmark, and EFSA Concise Database, 2008.

in Belgium. After a 4–5-year period of the intervention being in place, it is assumed that this number will decrease by about 38% to 924,353 adult persons with multinodular goiter and thyroid nodules, as was the case in Denmark.

For the estimation of direct, indirect, medical, and nonmedical TC in the adult population in Belgium, data from the Federal Public Service of Public Health, Food Chain Safety and Environment, the National Institute for Disease and Disability Insurance (RIZIV/INAMI), the Information Network about the prescription of reimbursable medicines (FARMANET), Intercontinental Marketing Services (IMS), and expert opinions were used. Only figures dating from before the start of the intervention (before 2009) were exploited.

To determine the percentage of persons undergoing surgery for multinodular goiter and thyroid nodules, data from the Federal Public Service of Health, Food Chain Safety and Environment were used. These include data from all seven insurance companies in Belgium and the public center for social welfare (OCMW). To calculate the costs of surgery and related costs (hospital stays), these data were linked with the data from RIZIV/INAMI, which include only data from all seven insurance companies in Belgium (excluding OCMW and insurance for invalid persons).

The number of adult persons ($\geq$18 years) undergoing surgery for multinodular goiter or thyroid nodules in Belgium was 4856 in 2003, 4925 in 2004, 4794 in 2005, 4814 in 2006, and 4973 in 2007, which resulted in a mean of 4873 per year or more or less 0.33% of the Belgian adult population suffering from thyroid nodular diseases. Only hospitalizations including thyroid nodular diseases as principal diagnosis were taken into account. Costs for surgery per year, over the years 2005–2007, including hospital stays, blood tests, metabolic therapy, pharmaceuticals, diagnosis, and clinical biology can be found in Table 2. The total average cost per year related to surgery for thyroid nodular diseases was estimated to be €13,128,807.

To assess the percentage of people with multinodular goiter or thyroid nodules going to the general practitioner or the specialist in the hospital, data about the number of adult persons ($\geq$18 years) using antithyroid medications (both reimbursed [FARMANET] and not reimbursed [IMS data] medication) and data about the number of persons undergoing I-131 treatment (RIZIV/INAMI) in the hospital were used.

Hormone treatment (such as with levothyroxine) is used mainly to treat hypothyroidism in Belgium. It is used much less frequently for multinodular goiter or thyroid nodules. Therefore data relating to this were not used in the analysis. In 2008 there were 20,313 adults ($\geq$18 years) in Belgium who were reimbursed for the use of antithyroid medications (58,196 packages of methimazole as thiamazol or Strumazol®). In addition, 45,436 packages of propylthiouracil (PTU) were used by adults in the same year and it was estimated that the average number of packages per person per year was 18. This medication is not reimbursed by the RIZIV/INAMI. The prevalence of hyperthyroidism due to Graves' disease in Denmark was $\sim$40%, whereas the prevalence of hyperthyroidism due to multinodular goiter was 50% (34). Therefore, it is estimated that 50% of the packages of methimazole and 50% of the packages of propylthiouracil were used to treat hyperthyroidism secondary to multinodular goiter or autonomous thyroid nodules in Belgium. Based on the number of packages of methimazole (either generic or brand name) whose cost was reimbursed in Belgium in 2008, the costs of these were estimated to be €320,228. Therefore, considering that half of the use of this drug was for thyrotoxic nodular thyroid disease, the reimbursement for the use of methimazole to treat thyrotoxic nodular thyroid disease was estimated to be €160,114.

I-131 therapy is widely used for the treatment of hyperthyroidism due to autonomous thyroid nodules and multinodular goiter in Belgium. It is used much less frequently for treatment of thyroid cancer and Graves' disease. The mean number of treatments with I-131 over the years 2003–2007 was 4300, with an average total cost per year of €979,537.

In addition to treatment costs, there are costs for the diagnosis and follow-up of multinodular goiter and thyroid nodules. The only available data are those for diagnosis and follow-up by specialists. General practitioners also follow patients with nodular thyroid diseases, but blood tests and other tests for diagnosis of thyroid diseases (ultrasound, thyroid scan, and thyroid uptake) are exclusively performed by specialists. Costs related to diagnosis and follow-up by specialists were received from RIZIV/INAMI. The average number of cases and the total related average costs of diagnosis and follow-up in a hospital setting for the period 2003–2007 are presented in Table 3. The total average cost per year related to diagnosis and follow-up by specialists of the abovementioned pathologies was estimated to be €23,267,693.

Results

The total annual TC caused by MID in the adult population in Belgium, including surgery (€13,128,807), diagnosis and follow-up (23,267,693), medicines and hormone treatment (€160,114), and I-131 treatment (€979,537) amounted to €37,536,151. The total PC in Belgium, including monitoring

TABLE 2. COSTS IN EUROS FOR SURGERY DUE TO THYROID NODULAR DISEASES IN BELGIUM 2005–2007

Year	*Number of hospital stays*	*Number of hospital days*	*A*	*B*	*Total costs*
2005	4712	20,785	€6,321,419	€6,088,117	€12,409,536
2006	4770	20,255	€6,490,184	€6,531,599	€13,021,783
2007	4946	20,199	€6,762,609	€7,192,494	€13,955,103
Av/Y	4809	20,413	€6,524,737	€6,604,070	€13,128,807

Av/Y, average costs per year; A, costs related to stays in the hospital; B, costs related to blood tests, metabolic therapy, use of pharmaceuticals, diagnosis tests, and clinical biology.
Source: Link between Data Federal Public Service of Health and RIZIV/INAMI.

Table 3. Average Yearly Costs in Euros of Diagnosis and Follow-Up of Thyroid Nodular Diseases by Specialists in Belgium 2003–2007

Test	Average number of cases	Average costs
Thyroid uptake	7964	€771,249
Thyroid scan	48,867	€4,788,432
Thyroid ultrasound	98,103	€2,320,209
TSH	4,034,666	€7,213,262
FT4	2,391,604	€5,985,205
FT3	764,540	€1,913,831
Anti-TPO	78,881	€140,035
Anti-thyroglobuline	76,312	€135,470
Total		€23,267,693

TSH, thyroid-stimulating hormone; FT4, free thyroxine; FT3, free triiodothyronine; TPO, thyroid peroxidase.
Source: RIZIV/INAMI.

(€260,000) and social marketing (€10,000), were estimated to be €270,000 over a 4–5-year period (Table 4).

To calculate the saved costs per year after a 4-year period having the iodization program in place, it was assumed that prevalence of multinodular goiter and thyroid nodules will decrease by 38% in Belgium as was the case in Denmark with a similar intervention in place (33). The net saved costs per year, due to the optimization of iodine intake in Belgium, can consequently be calculated as follows:

$0.38\times$(total TC in the adult population in Belgium) $-$ (total PC including monitoring/5) $= 0.38\times$€37,536,151 $-$ €270,000/5 $=$ €14,209,737 (Tables 4 and 5).

Discussion

Our analysis indicates that the saved costs after the implementation of an iodization program in a country suffering from MID can be considerable. In this study in Belgium the net benefit of such a program would be around €14 million. Nevertheless, these findings have to be interpreted with caution. One of the limitations of this study is that prevalence data from another country were used to perform the calculations. In future, efforts should be undertaken to collect prevalence data on thyroid nodular diseases in Belgium. Further, it needs to be stressed that many costs were not included, such as costs due to better cognition and higher productivity, and costs due to work disability (absence from work), as specified in the methods section, but it makes the estimation reliable and conservative.

It should be noted also that only 1.8% of the adult persons suffering from thyroid nodules or multinodular goiter are treated with antithyroid medication or I-131 iodine therapy and only 0.33% undergo surgery. This indicates that a high number of adult persons are probably not aware that they have nodular thyroid disease.

Table 4. Costs Related to the Iodization Program in Belgium

Part of the program	Average costs
National survey in school-aged children and pregnant women	€260,000
Monitoring of TSH in newborns	0
Leaflet for pregnant women	€10,000
Monitoring of iodine content in salt used for manufacture of bread	0
Total	€270,000

Table 5. Summary of Total Average Yearly Costs Related to the Iodization Program and Thyroid Nodular Diseases in Belgium

	Average costs
Monitoring program	€54,000
Surgery	€13,128,807
Treatment (anti-thyroid medication and I-131 therapy)	€1,139,651
Diagnosis and follow-up by specialists	€23,267,693

Conclusion

The yearly costs related to MID in the Belgian adult population are $\sim$€38 million. It is expected that the iodization program will decrease the prevalence of thyroid nodular disease with 38% after a 4–5-year period. Due to this, it will be possible to save at least €14 million a year.

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Disclosure Statement

The authors declare not having any conflicts of interest. No competing financial interests exist.

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